Title: Older Patients' Prescriptions Screening in the Community Pharmacy: Development of the Ghent Older People's Prescriptions Community Pharmacy Screening (GheOP3S) Tool

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Older patients' prescriptions screening in the community pharmacy: development of the Ghent Older People's Prescriptions community Pharmacy Screening (GheOP³S) tool

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ABSTRACT

Background. Aging of the population often leads to polypharmacy. Consequently, Potentially Inappropriate Prescribing (PIP) becomes more frequent. Systematic screening for PIP in older patients in primary care could yield a large improvement in health outcomes, possibly an important task for community pharmacists. In this manuscript, we develop an explicit screening tool to detect relevant PIP that can be used in the typical community pharmacy practice, adapted to the European market.

Methods. Eleven panellists participated in a two-round RAND/UCLA (Research and Development/University of California, Los Angeles) process, including a round zero meeting, a literature review, a first written evaluation round, a second face-to-face evaluation round, and finally, a selection of those items that are applicable in the contemporary community pharmacy.

Results. Eighteen published lists of PIP for older patients were retrieved from the literature, mentioning 398 different items. After the two-round RAND/UCLA process, 99 clinically relevant items were considered suitable to screen for in a community pharmacy practice. A panel of seven community pharmacists selected 83 items, feasible in the contemporary community pharmacy practice, defining the final GheOP³S-tool.

Conclusion. A novel explicit screening tool (GheOP³S) was developed to be used for PIP-screening in the typical community pharmacy practice.

KEYWORDS: Screening, Primary care, Health services

KEY POINTS

- The GheOP³S-tool is the first explicit screening tool, specifically designed for use in the community pharmacy practice.
- Identification of PIP in the community pharmacy practice is aimed at facilitating pharmacist discussion with patients and health care providers
- Using the GheOP³S-tool, community pharmacists could play a supportive role in a prescription process in which the most beneficial and clinically effective medication with the lowest possible risk for adverse drug events is delivered to the older patient.

INTRODUCTION

The population of older patients is increasing in most European countries(1). Because of co-morbidities and polypharmacy, in addition to age-related changes in pharmacokinetics and pharmacodynamics, older patients are more at risk for adverse drug events (ADEs), leading to increased morbidity, mortality and financial costs(2, 3). ADE prevalence has been shown to be associated with Potentially Inappropriate Prescribing (PIP)(4). PIP comprises overuse, underuse and misuse of drugs(5) and is thus a potential, though indirect, cause for increased social and economic burden(1, 6). Despite increasing awareness of PIP in older patients and its consequences, PIP prevalence remains high(7, 8).

Several interventions aiming to reduce PIP in older patients have been proposed and evaluated(9). Most of these interventions apply an approach that involves a (clinical) pharmacist who initiates a screening process using a specifically developed screening tool(9). However, most of these screening tools have been designed and validated solely in hospitals or nursing home settings(10-23), and often require clinical and laboratory information, usually unavailable to the community pharmacist. Therefore, studies that investigate PIP in primary care need to either modify or can only use portions of existing screening criteria(24-27). Furthermore, some screening tools lack scientific evidence, are not yet validated in clinical practice, do not offer alternative therapeutic options or are not adapted to the European market(10-12, 22). Yet, it seems reasonable that systematic screening for PIP in older patients in primary care could yield a large improvement in health outcomes(28).

The community pharmacist may be ideally placed to engage in this process because of his medication-specific knowledge and because of the availability of an electronic dispensing record in the pharmacy. However, this engagement would require an evidence-based and feasible screening tool specifically suitable for use in the typical community pharmacy practice. Such a tool, to the best of our knowledge, has not yet been developed. In this manuscript, we therefore present the development of the GheOP³S-tool: the Ghent Older People's Prescriptions community Pharmacy Screening tool.

METHODS

Design summary

The GheOP³S-tool was developed in five steps, based on the RAND/UCLA (Research and Development/University of California Los Angeles) method(29). It included (i) a round zero meeting, (ii) a literature review, (iii) a first written Delphi round, (iv) a second face-to-face Delphi round based on the first round evaluation, and (v) finally, a selection of those items considered applicable in the contemporary community pharmacy practice.

Round zero meeting

In the round zero meeting the research team (ET, MP, AS, EM, KB) reached consensus on the working procedures, and on a 5-part structure for the GheOP³S-tool: Part 1: Potentially inappropriate drugs, independent of diagnosis, Part 2: Potentially inappropriate drugs, dependent on diagnosis, Part 3: Potential Prescribing Omissions (PPOs), Part 4: Drug-Drug Interactions (DDIs) of specific relevance and Part 5: General care-related items to be addressed in the community pharmacy (Table 1). This structure was deliberately chosen to make community pharmacists familiar with the existence of different types of PIP (underuse, overuse and misuse). Furthermore, this structure offers the opportunity of a stepwise implementation of the tool.

Literature review

To identify previously developed screening tools for the detection of PIP in older adults, a literature search was performed within the PubMed database, using following terms and/or combinations: “elderly”, “older age”, “Aged”, “inappropriate prescribing”, “inappropriate medication”, “protocol”, ”criteria” and “screening tool”. All articles published between January 1990 and December 2012 were eligible if they contained explicit criteria addressing inappropriate prescribing in older patients. For lists that were updated (such as Beers List), only the most recent version was included. References of included articles were manually searched for completeness.

A total of 18 explicit lists were retrieved (10-23, 30-33) and summarized. All mentioned items were classified into the 5-part-structure of the GheOP³S-tool. Criteria to withhold items for evaluation by the Delphi-panel were determined for each part of the tool (See Appendix 1). This way, a literature-based list of potential items for the tool was created. Furthermore, the literature review was extended with an up-to-date summary of the best available scientific evidence regarding all withheld items. Where evidence from randomized controlled trials was missing, the review also included lower quality of evidence. Additionally, for each PIP item, an alternative therapeutic option was offered, relying on existing evidence.

First Delphi round: written individual evaluation

The research team invited a 12-person multidisciplinary Delphi panel encompassing all decision-making disciplines involved in geriatric care, including 4 clinical pharmacists, 2 geriatricians, 2 general practitioners, 2

academics, one community pharmacist, and an emergency physician. Eleven panellists from various European countries agreed to participate. The main selection criteria for panellists were acknowledged leadership in the panel member's specialty, absence of conflicts of interest, geographic diversity and diversity of practice setting.

In February 2013, all participating panellists were provided with the literature review and a scoring form. For each item, panellists were asked to reply to the following questions considering scientific evidence from the literature review and using their best clinical judgement: "How do you rate the added clinical value of a check on this item for an older patient by the community pharmacist?" and "How do you rate the proposed alternative?". Prescribing and sales data of the proposed items were available to the panellists upon request. Practical aspects considering the organization of community pharmacies in the panellist's country and cost implications were on the other hand specifically instructed to be excluded in making this judgement (e.g., access to patients' clinical records at the community pharmacy had not be taken into account). All items were scored on a scale, ranging from 1 to 9, with 1 indicating that checking for this item in the community pharmacy has no added clinical value or the proposed alternative was not appropriate. A score of 9 indicated that checking for this item in the community pharmacy has a high added clinical value or that the proposed alternative is highly appropriate.

After summarizing all panellists' individual ratings a preliminary list of clinically relevant items for the tool was created, consisting of all items with a median score in the 7-9 range and all items rated "with disagreement". To define "disagreement" we used the previously developed "D9R" definition: "considering all ratings, at least one falls in the lowest 3-point region and at least one falls in the highest". We controlled results with the IPRAS method described in the RAND/UCLA user manual, however no discrepancies were detected(29).

The panellists were also offered the possibility to add items and to suggest alternative treatments, which, to their judgement, would form a positive contribution to the screening tool. A summary of these items was made and the evidence supporting the suggested items was collected. These suggestions were also added to the preliminary list. Panellists were provided with the complete preliminary list of clinically relevant items for the tool two weeks prior to the second Delphi round. Only items scored with disagreement and suggested items or alternative treatments were to be discussed in the second Delphi round.

Second Delphi round: face-to-face meeting

During the second Delphi round in May 2013, all participating panellists were provided with their individual ratings and the ratings of the other group members. One general practitioner, one clinical pharmacist and one emergency physician could not attend, resulting in an 8-member panel. The moderator specifically focused the discussion on newly suggested items and on items for which there was "disagreement" among the panellists, as described in the RAND/UCLA manual(29). After discussing each part of the preliminary list of clinically relevant items for the GheOP^{3}S-tool, panellists were asked to re-rate the items. No attempt was made to force panellists to consensus.

The same summarizing method was used as in the first Delphi round, with the exception that all items rated "with disagreement" at this stage were deleted from the list. This resulted in a *final list of clinically relevant items for the tool*, which was sent out to all panellists for final approval.

Retaining items applicable in contemporary community pharmacy practice

Finally, the research team invited a panel of 7 Belgian community pharmacists to select those items that were applicable in the contemporary community pharmacy practice, using the same methodology as in steps 3 and 4: a two-round Delphi consisting of a first written round and a second verbal round. Panellists were asked the following question "How do you rate the feasibility of a check on this item in the current community pharmacy practice?" and "How do you rate the feasibility of the proposed alternative strategy?". To clarify that the goal of this developmental stadium was merely a selection of items that are presently applicable, pharmacists were instructed to consider practical aspects of pharmacy workflow and cost implications rather than assess the clinical relevance of each item.

RESULTS

Literature review

Eighteen published lists of potentially inappropriate medications for older patients were retrieved from the literature, mentioning a total of 398 different items, each of them categorized in one of the predefined parts of the GheOP³S-tool. After applying selection criteria mentioned in Appendix 1 (e.g., availability in at least 4 European countries), a total of 121 items were retained, each complemented with the best available scientific evidence considering older patients. The specific lists used for each part of the GheOP³S-tool are displayed in Table 3. The flow of the items through the development process is shown in Table 4.

First Delphi round: written individual evaluation

In the first Delphi round, panellists reached immediate consensus on 73 of the 121 literature-based items (Part 1: 33/53; Part 2: 21/33; Part 3: 5/7; Part 4: 12/24 and Part 5: 2/4), leaving 48 items for discussion in the second Delphi round. Furthermore, an additional 28 items were proposed by the panellists. Only one item concerning loperamide was considered of no clinical relevance and was omitted from the preliminary list of items for the tool. 53 of the 121 alternative therapeutic options were rated with disagreement and were also to be discussed in the second Delphi round.

Second Delphi round: face-to-face meeting

During the second Delphi round, all items rated "with disagreement" after the first round (48 items) were discussed as well as the 28 additional panellist-proposed items. The panel decided to group some of the items together (e.g. instead of including all individually named long-acting sulfonylurea derivatives such as glibenclamide and glimepiride, a new item was created: "Any long-acting sulfonylurea derivative") (Table 1 Part 1a). After discussion, consensus was reached for all proposed alternatives. After sending out the final list of 99 clinically relevant items and their therapeutic alternatives for approval, no further changes were requested by participating panellists.

Retaining items applicable in contemporary community pharmacy practice

The panel of community pharmacists selected 83 items that they found to be applicable in the contemporary community pharmacy setting. One DDI was divided into two different items because of feasibility of the management plan (oral antidiabetic/insulin + beta blocker replaced by: oral antidiabetic/insulin + non-selective beta-blocker and oral antidiabetic/insulin + cardioselective beta-blocker). The 83 items define the final GheOP³S-tool (Table 1 and Table 2). For all of these items, extended information with rationales, management plans and scientific literature was compiled (currently only available in Dutch and French(34)). Items with clinical relevance for primary care, but not (yet) applicable in the community pharmacy practice, are displayed in Table 5.

DISCUSSION

Main finding of this study

In this study, we developed the GheOP³S-tool, a screening tool consisting of 83 items for identifying PIP in older patients in the community pharmacy practice. The items of the GheOP³S-tool were categorized in 5 different parts: Part 1: Potentially inappropriate drugs, independent of diagnosis, Part 2: Potentially inappropriate drugs, dependent on diagnosis, Part 3: PPOs, Part 4: DDIs of specific relevance and Part 5: General care-related items to be addressed in the community pharmacy (Table 1 and Table 2). For every item, an alternative therapeutic option was offered.

What is already known on this topic

Worldwide, the need for PIP-screening is rising in order to reduce prevalence of ADE(35, 36). As PIP-screening is part of pharmaceutical care, it is an assigned task of the community pharmacist(37, 38). Therefore, it is surprising that screening tools, specifically developed for this setting, are lacking. Community pharmacists have nevertheless shown to be effective in detecting PIP, even when non-specific or adapted tools were used(9, 25, 39). The access to both the over the counter (OTC) and prescription medication record is also a major benefit, as missing OTC-data is an established risk factor for overlooking PIP in older patients(40). Moreover, including a pharmacist in a multidisciplinary team to approach a patient's pharmacotherapy has been shown to be the safest and most rational way of prescribing(9).

What this study adds

An ideal screening tool for routine use in community pharmacy practice should be user-friendly, evidence-based, inexpensive to apply and interchangeable between countries. To meet these requirements, the GheOP³S-tool was developed as an explicit screening tool designed for community pharmacists. Where practical issues with implicit lists may arise (i.e. often lacking the necessary clinical and laboratory information), an explicit screening tool provides community pharmacists with a reference that supports pragmatic PIP-screening in a systematic and straightforward way. Moreover, the explicit character of the GheOP³S-tool allows future automatisation of the screening, giving pharmacists the time to focus on checking patient-specific relevance, on inter-care giver communication and on drawing up a management plan. Furthermore, the grouping of items in Part 1a (e.g., "any non-steroidal anti-inflammatory drug (NSAID)" instead of naming each locally marketed NSAID) facilitates transition between countries, where different drugs in a particular drug class are available. Additionally, it anticipates the commercialisation of new molecules that were not yet marketed at the time of the tool-development.

A unique aspect of the GheOP³S-tool is the incorporation of a subset of items that evaluates the delivery of pharmaceutical care to the community-dwelling older patient (Table 1, Part 5: "General care-related items to be addressed in the community pharmacy"). In this section, the community pharmacist checks in an implicit

way whether sufficient basic pharmaceutical care is provided. This includes – for example – verifying the need for a medication scheme or a regular evaluation of the medication adherence.

Limitations of this study

The development of the presented GheOP³S-tool using the RAND/UCLA methodology has some limitations. However, the methodological quality of the development was guaranteed by a thorough selection of the participating experts, extended scientific evidence for all included items and information about prevalence of ADEs attributable to PIP. Moreover, the setting in which the tool should be used was sufficiently taken into account by adding an extra step in the development process and by providing panellists with access to prescribing and sales data of the proposed items. Because the GheOP³S-tool is designed for routine implementation, it is evident that also a feasibility study, which in the meantime has been initiated, is necessary. Additionally, as well as for all explicit screening tools, it is stressed that the screening is aimed at assisting in clinical decision making for the older patients and not at making the decision on its own. We emphasize that an eventual adaptation of the treatment plan remains the result of a shared decision-making process. Finally, although all currently employed pharmacists have an adequate education in pharmacology, basic pathophysiology, basic diagnostic testing and pharmacotherapy, PIP-screening, on the other hand, was barely a part of the curriculum. The delivery of continuing post-academic professional development will therefore be a prerequisite for the correct implementation of the GheOP³S-tool and correct interpretation of results.

Implications for future research

Since the GheOP³S-tool is specifically developed for use in the community pharmacy, it could address previously described and widely spread PIPs in community-dwelling older patients, such as long-term proton pump inhibitors (PPI) or benzodiazepine use(41-43). As previous trials have shown that screening for PIP could have a positive clinical and economic impact(44, 45), a routine use of the GheOP³S-tool in the community pharmacy practice could have an impact on patient's health and health care budgets. A future (cost-) effectiveness trial should therefore study the efficacy of a screening with the GheOP³S-tool by a community pharmacist on patient centred outcomes (i.e. hospital admissions, utilisation of health care resources, etc.). This way, the clinical and content validity of the screening tool as well as the efficacy of screening would be evaluated. Since polypharmacy and older age are major risk factors for PIPs and ADEs(24, 46), it is desirable to focus such a trial on an older population taking five or more drugs a day. However, if (limited) laboratory data such as renal function, would be available in trial context or in the community pharmacy because of policy changes, items from Table 5 can be added to the GheOP³S-tool.

CONCLUSION

The GheOP³S-tool is the first explicit screening tool, specifically designed for use in the community pharmacy practice. The developmental design of the GheOP³S-tool offers a high flexibility in terms of adding or modifying specific parts of the tool. The GheOP³S-tool is intended to be used for PIP-screening in routine community pharmacy practice and to facilitate patient and caregiver communication. Using this tool, community pharmacists could play a supportive role as an advocate for the patient in which the most beneficial and clinically effective medication with the lowest possible risk for ADEs is delivered. Future research is required to determine whether screening for PIP with this tool results in detection of clinically relevant drug related problems and in optimization of drug therapy for older patients and whether it can reduce the cost of PIP.

Appendix 1:

Criteria to withhold items in Part 1 (Potentially inappropriate medication for older patients, independent of diagnosis)

Starting from all existing lists with explicit criteria on potentially inappropriate medication for older patients, independent of diagnosis, we withheld all items that were mentioned on at least 4 lists, as well as all OTC-available drugs mentioned on at least 1 list. Subsequently, we retained only those items considering drugs that are available in at least 4 European countries.

Criteria to withhold items in Part 2 (Potentially inappropriate medication for older patients, dependent on diagnosis)

Starting from all existing lists with explicit criteria on potentially inappropriate medication for older patients with certain diseases, we withheld all items mentioned on ≥2 lists. Items considering drugs not available in at least 4 European countries were deleted. Because of clinical relevance, 10 recommendations of the Koninklijke Nederlandse Maatschappij ter bevordering der Pharmacie (KNMP)(32) and the HARM-Wrestling report(31) concerning drugs administered in patients with renal impairment were added to the list.

Criteria to withhold items in Part 3 (Potential Prescribing Omissions)

Starting from all existing lists with explicit criteria on potential prescribing omissions in older patients, we only withheld items confirmed by recommendations of the HARM-Wrestling report[31] or ACOVE quality indicators[30]. Items considering drugs not available in at least 4 European countries were deleted.

Criteria to withhold items in Part 4 (Drug-Drug interactions of specific relevance in older patients)

Starting from all existing lists with explicit criteria on drug-drug interactions (DDI) of specific relevance in older patients, we only withheld DDIs of which clinical relevance in older patients was confirmed through the HARM-Wrestling report[31] or the systematic review of Hines et al[33]. DDIs considering drugs not available in at least 4 European countries were deleted.

Criteria to withhold items in Part 5 (General care-related items for older patients to be addressed in the community pharmacy)

Starting from all existing lists with explicit criteria on General care-related items for older patients to be addressed in the pharmacy, we withheld items if they have a contribution to drug-related problems (e.g. recording of fall frequency and long-term benzodiazepine use). None of the lists mentioned care-centred items. However, ACOVE-criteria[30] and the HARM-Wrestling report[31] mentioned four care-related items. For each of these statements, scientific evidence for being on the list was evaluated.

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None

COMPETING INTERESTS

All authors completed the ICMJE-form. No competing interests were declared.

Tables

Table 1: The GheOP³S-tool

Table 2: Drugs with high risk for anticholinergic (side-)effects (Adapted from Duran et al. (47))

Table 3: Published lists, used as basis for the GheOP³S-tool.

Table 4: Flow of the items through the development process of the GheOP³S-tool.

Table 5: Items deleted from each GheOP³S-part because of current inapplicability in the community pharmacy

Table 1: The GheOP³S-tool		
Part 1a: Potentially inappropriate drugs, independent of diagnosis - Drug classes		
No.	Item	Alternative
1	Any antidepressant ≥1year	Check if indication is still present, if not: discontinue therapy If therapy is continued: check co-medication
2	Any antipsychotic drug ≥1 month	1st Consider need for chronic use (≈ Is original indication still present?) , if not: discontinue therapy 2nd Always consider non-pharmacological approach
3	Any drug for arterial vascular disorders	Therapeutic abstention Recommend non-pharmacological approach (compression hosiery, discuss referral to surgery with GP, physiotherapy...).
4	Any intermediate acting benzodiazepine or Z-product at full dose or any dose ≥30 subsequent days	- For sleeping disorders: Startup: 1st Consider non-pharmacological approach 2nd Prefer intermediate acting benzodiazepine or Z-product at 1/2 dose of young adults >30 subsequent days: Consider non-pharmacological approach (sleep hygiene), provide GP with withdrawal plan and assure GP of support by pharmacists in withdrawal - For anxiety: consider non-pharmacological approach and switching to SSRI
5	Any short or long-acting benzodiazepine	- Startup: 1st Consider non-pharmacological approach 2nd Prefer intermediate acting benzodiazepine or Z-product at 1/2 dose of young adults <30 subsequent days - Chronic: Consider non-pharmacological approach (sleep hygiene), provide GP with withdrawal plan and assure GP of support by pharmacists in withdrawal
6	Any long-acting sulfonylurea derivative	Metformin or any short-acting sulfonylurea derivative
7	Any nasal vasoconstrictor ≥1 month	Hypertonic saline solution or referral to GP
8	Any oral NSAID	Consider need for anti-inflammatory therapy. If possible: paracetamol or stronger non-NSAID (eg. opioid) is safer choice If therapy is considered necessary, prefer low dose ibuprofen. Avoid NSAIDs with high GI-risk (piroxicam, ketorolac) Prefer ibuprofen/naproxen when CV-risk Prefer NSAIDs with short half-life (ibuprofen, diclofenac) Always add gastroprotection (most evidence for PPI in standard dose) Closely monitor renal function or blood pressure depending on present diagnoses
9	Any PPI at full dose[a] ≥8 weeks	Consider need for chronic use and reduce dose if possible
10	Any recently marketed drug (black triangles)	Consider using drug with similar indication and more evidence in older patients
11	Any sedating antihistaminic drug	1st Verify indication, if not valid: stop therapy or switch to appropriate therapy 2nd If indication is valid: switch to non-sedating antihistaminic drug
Part 1b: Potentially inappropriate drugs, independent of diagnosis - Specific molecules		
12	Alizapride	Non pharmacological approach, if not sufficient: Reduce dose to 3 x 25 mg/day
13	Bisacodyl	Macrogol/lactulose
14	Clonidine	Consider other safer antihypertensive
15	Codeine and its derivatives for acute cough	Therapeutic abstention or safer alternative (eg., honey)
16	Dabigatran	Warfarin/Acetylsalicylic acid/Heparin, depending on indication
17	Digoxin >0,125mg/day	Digoxin ≤0,125mg/day or serum level between 0,5 and 0,8 µg/L
18	Dipyridamole monotherapy (without ASA)	Acetylsalicylic acid in low dose
19	Ginkgo biloba or Panax ginseng	Referral depending on underlying condition.
20	Liquid paraffin	Macrogol/lactulose
21	Methyldopa	Consider other safer antihypertensive
22	Metoclopramide	Non pharmacological approach, if not sufficient: Reduce dose to 3 X 5 mg/day
23	Pentazocine	Consider paracetamol/codeine combination or pure morphinomimetic agent, depending on indication
24	Phenobarbital	Verify that GP checked diagnosis with prescribing neurologist
25	Pseudoephedrine oral	Short-term intranasal therapy (nasal vasoconstrictor <7 days or hypertonic saline solution)
26	Rivaroxaban or Apixaban	Warfarin/Acetylsalicylic acid/Heparin, depending on indication
27	Senna glycosides	Macrogol/lactulose
28	Picosulfate	Macrogol/lactulose
29	Theophylline	Reconsider indication, preferably stop theophylline
30	Ticlopidine, new prescription	Verify indication, prefer safer alternative
31	Tramadol, new prescription	Check if step-up approach was used. Paracetamol/Codeine could be more appropriate
Part 2a: Potentially inappropriate drugs, dependent on diagnosis - Drug classes		
32	Any antipsychotic other than quetiapine and clozapine with Parkinson's disease	Quetiapine and clozapine are preferred: they appear to be less likely to precipitate worsening of Parkinson's disease
33	Anticholinergics (e.g. Antihistamines, Antidepressants, Antipsychotics, Antispasmodics…) (cfr Table 2) with dementia or cognitive impairment	Consider drug for same indication with less or none anticholinergic activity (cfr Table 2)
34	Anticholinergics (e.g. Antihistamines, Antidepressants, Antipsychotics, Antispasmodics…) (cfr Table 2) with constipation	Consider drug for same indication with less or none anticholinergic activity (cfr Table 2) If therapy is necessary: add osmotic laxative and apply non-pharmacological measures
35	Anticholinergics (e.g. Antihistamines, Antidepressants, Antipsychotics, Antispasmodics…) (cfr Table 2) with BPH	Consider drug for same indication with less or none anticholinergic activity (cfr Table 2) If therapy is necessary: check urinary residue shortly after start with anticholinergic drug. Recheck when suspicion of urine retention.
36	Calcium Channel Blockers with constipation	Prefer class of antihypertensive agent that hasn't constipation as side-effect If calcium channel blocker is necessary, prefer dihydropyridines (amlodipine) and/or add osmotic laxative
37	Non-selective beta-blockers with asthma or COPD	Consider cardioselective beta-blocker or other class of antihypertensive drugs

38	Oral corticosteroids >1 week with diabetes	Closely monitor glycemic control and blood pressure Shorten therapy duration as much as possible Always warn patient about possible dysregulation
39	Oral corticosteroids >1 week with hypertension	Closely monitor blood pressure and glycemic control Shorten therapy duration as much as possible Always warn patient about possible dysregulation
40	Thiazide and loop diuretics with gout	Prefer other class of antihypertensive drugs If diuretic is necessary; prefer potassium sparing (pay attention to renal impairment and probable interactions)
Part 2b: Potentially inappropriate drugs, dependent on diagnosis - Specific molecules		
41	Alizapride with Parkinson's disease	1st Always apply non-drug and diet therapy. 2nd If anti-emetic therapy is necessary, prefer domperidone in low dose only if no cardiac risk factors are present and no other QT-prolonging drugs are used
42	Metoclopramide with Parkinson's disease	1st Always apply non-drug and diet therapy. 2nd If anti-emetic therapy is necessary, prefer domperidone in low dose only if no cardiac risk factors are present and no other QT-prolonging drugs are used
Part 3: Potential prescribing omissions		
43	The patient is taking ≥ an equivalent of 7.5 mg of oral prednisone for ≥3 months and is not prescribed Ca/VitD supplementation and bisphosphonates.	
44	The patient is taking narcotic analgesics and is not prescribed appropriate preventative bowel regimen (preferably macrogol or lactulose).	
45	The patient has an elevated risk for osteoporosis (determined via FRAX-tool(48)) and is not prescribed Calcium/Vitamin D supplementation.	
46	The patient is taking oral corticosteroids for ≥1 month and is not prescribed Ca/VitD supplementation.	
47	The patient is not reminded and proposed to undergo yearly influenza vaccination.	
48	The patient is taking methotrexate and is not prescribed folic acid supplementation.	
Part 4: Drug-Drug interactions of specific relevance		
49	VKA + oral NSAIDs	1st Consider need for NSAID. If possible: paracetamol or stronger non-NSAID (eg. opioid) is safer choice 2nd If NSAID is unavoidable, prefer low dose ibuprofen, but always add gastroprotection (most evidence for PPI in standard dose) and keep in mind to closely monitor renal function or blood pressure depending on present diagnoses
50	RAAS-inhibitor + potassium sparing diuretic/potassium supplements/potassium containing drugs[b]	1st Preferably change to non-potassium sparing diuretic/switch to non-potassium containing drug equivalent 2nd If combination is unavoidable: monitor renal function and serum potassium and always inform patient about symptoms of hyperkalaemia
51	VKA + Antiplatelet drugs (esp. ASA), unless prescribed by internist/cardiologist	1st Check if combination is appropriate (artificial valve, up to 3 months after acute coronary syndrome and for rheumatic mitral valve stenosis) 2nd When combination is not appropriate: stop ASA and monitor INR
52	VKA + TMP/SMX	1st Preferably switch to other antibiotic based on indication 2nd If combination is unavoidable: monitor INR
53	Oral NSAID + Oral Corticosteroids	1st Consider need for NSAID. If possible: paracetamol or stronger non-NSAID (eg. opioid) is safer choice 2nd If NSAID is unavoidable, prefer low dose ibuprofen, but always add gastroprotection (most evidence for PPI in standard dose) and keep in mind to closely monitor renal function or blood pressure depending on present diagnoses
54	Oral NSAID + Diuretic	1st Consider need for NSAID. If possible: paracetamol or stronger non-NSAID (eg. opioid) is safer choice 2nd If NSAID is unavoidable: monitor renal function, blood pressure and serum potassium
55	Digoxin + Macrolide antibiotics	1st Preferably switch to other antibiotic based on indication 2nd If combination is unavoidable: monitor serum digoxin levels and always inform patient about signs of digoxin toxicity
56	Digoxin + Verapamil/Diltiazem	1st Starting digoxin: use lowest possible dose 2nd Starting diltiazem: check serum digoxin levels for 1 to 2 weeks 3rd Starting verapamil: lower digoxin dose to 50-70% of usual dose + check serum digoxin levels for 1 to 2 weeks 4th Altering dose of verapamil/diltiazem: alter digoxin dose using serum digoxin levels Always inform patient about signs of digoxin toxicity
57	Lithium + RAAS-inhibitors	1st Consider need for RAAS-inhibitor 2nd If combination is unavoidable: monitor lithium levels within 3-5 days after starting RAAS-inhibitor and always inform patient about signs of lithium toxicity
58	Lithium + Oral NSAID	1st Consider need for NSAID. If possible: paracetamol or stronger non-NSAID (eg. opioid) is safer choice 2nd If combination is unavoidable: determine lithium levels before starting NSAID, give NSAID with strict schedule, check lithium levels after 3 days and modify intake dosage. Act similarly when NSAID is stopped and always inform patient about signs of lithium toxicity
59	Lithium + Diuretics	1st Consider need for diuretic. If possible: replace with appropriate alternative. 2nd If combination is unavoidable: determine lithium levels before starting diuretic, avoid 'on demand' use of diuretic, determine lithium levels after 3 days and modify intake dosage. Act similarly when diuretic is stopped and always inform patient about signs of lithium toxicity
60	Theophylline + Quinolones/Macrolides	1st Consider switching to other antibiotic based on indication 2nd If combination is unavoidable: monitor theophylline levels and always consider stopping theophylline
61	RAAS-inhibitor + Oral NSAID	1st Consider need for NSAID. If possible: paracetamol or stronger non-NSAID (eg. opioid) is safer choice. 2nd If NSAID is unavoidable: monitor renal function, blood pressure and serum potassium
62	Oral NSAID + SSRI/SNRI	1st Consider need for NSAID. If possible: paracetamol or stronger non-NSAID (eg. opioid) is safer choice 2nd If NSAID is unavoidable, prefer low dose ibuprofen, but always add gastroprotection (most evidence for PPI in standard dose) and keep in mind to closely monitor renal function or blood pressure depending on present diagnoses
63	RAAS-inhibitor + TMP/SMX	1st Preferably switch to other antibiotic based on indication 2nd If combination is unavoidable: monitor renal function and potassium level
64	Oral antidiabetics/insulin + non-selective beta-blocker	1st Always change to cardioselective beta-blocker (also relevant for eye drops) 2nd Inform patient about possible changes in awareness of hypoglycaemia
65	Oral antidiabetics/insulin + cardioselective beta-blocker	1st Consider need for beta-blocker + check glycemic control

		2nd Inform patient about possible changes in awareness of hypoglycaemia
66	Alprazolam/Midazolam/Triazolam/Zolpidem/Zopiclone + Strong CYP3A4 inhibitor	1st Preferably stop benzodiazepine use during treatment with CYP3A4 inhibitor 2nd Switch to equivalent drug with less or without CYP3A4 inhibiting activity
67	CCB + Strong CYP3A4 inhibitor	Preferably switch to equivalent drug with less or without CYP3A4 inhibiting activity
68	Oral NSAID + Antipletelet drugs	1st Consider need for NSAID. If possible: paracetamol or stronger non-NSAID (eg. opioid) is safer choice 2nd If NSAID is unavoidable, prefer low dose ibuprofen, but always add gastroprotection (most evidence for PPI in standard dose) and keep in mind to closely monitor renal function or blood pressure depending on present diagnoses
69	Phenytoin + TMP/SMX	1st Preferably switch to other antibiotic based on indication 2nd If combination is unavoidable: monitor phenytoin levels
70	First dose RAAS-inhibitor at full dosage + pre-treatment with diuretic	1st Start RAAS-inhibitor in lowest possible dose for 3 days 2nd Always give RAAS-inhibitor first 3 days at night and diuretic in the morning 3rd Always inform patient about possible orthostatic effect
71	Tamoxifen + strong CYP2D6 inhibitors	Prefer equivalent drug with less or without CYP2D6 inhibiting activity
72	Calcium + Quinolones/Tetracyclines	1st Use Calcium minimum 2 hours after quinolone/tetracycline or take quinolone/tetracycline 6 hours after intake of Calcium 2nd If not possible: Stop calcium
73	Calcium + Stontium ranelate	1st Use Calcium minimum 2 hours after strontium ranelate or take strontium ranelate 6 hours after intake of Calcium 2nd If not possible: Stop calcium
74	Calcium + Levothyroxine	1st Use Calcium minimum 2 hours after levothyroxine drug or take levothyroxine 6 hours after intake of Calcium 2nd If not possible: Stop calcium
75	Bisphosphonate + Calcium, Magnesium, Zinc, Iron or Aluminium	1st Use complexing agent minimum 2 hours after bisphosphonate 2nd If not possible: Switch to equivalent drug without complexing activity
76	VKA + Vitamin K containing drugs/supplements[c]	1st Switch to equivalent drug/supplement without Vitamin K 2nd If not possible: Monitor INR
77	Any combination of anticholinergic drug	1st Replace 1 of the drugs by an equivalent with less or without anticholinergic activity 2nd Always advise patients to report anticholinergic side-effects
Part 5: General care-related items to be addressed in the community pharmacy		
78	Dispensation of over-the-counter medication (NSAID, ASA…) was not added in the electronic patient record.	
79	Contra-indications that can unambiguously be derived from patient's medication were not added to the electronic patient record.	
80	Availability of assistance in medication/health issues (by nurse, neighbour, children etc.) was not checked nor discussed in frail older patients or older patients with reduced cognition, especially when taking drugs needing strict intake scheme.	
81	The patient was not asked which aspects of pharmaceutical care could be improved for him/her (Translated into practical questions for the specific patient: e.g. correct inhaler use, splitting tablets…).	
82	Adherence for all chronic medication was not checked or discussed during the past year (refill rate). Adherence for all new medication was not checked or discussed at first refill during the past year?	
83	Polypharmacy patients (chronically taking ≥ 5 drugs) were not questioned about whether a clear medication scheme was available to him/her.	

***ASA**: Acetylsalicylic acid; **BPH**: Benign prostatic hyperplasia; **CCB**: Calcium Channel Blocker; **COPD**: Chronic Obstructive Pulmonary Disease; **CV-risk**: Cardiovascular risk; **GI-risk**: Gastro-intestinal risk; **GP**: General Practitioner; **NSAID**: Non Steroidal Anti-Inflammatory Drug; **INR**: International Normalized Ratio; **PPI**: Proton Pump Inhibitor; **RAAS-inhibitor**: Renin-Angiotensin-Aldosteron System Inhibitors; **SNRI**: Serotonin and Noradrenalin Reuptake Inhibitor; **SSRI**: Selective Serotonin Reuptake Inhibitor; **TMP/SMX**: Trimetoprim/Sulfamethoxazol; **VKA**: Vitamin K Antagonist.*

[a] Full dose defined as: >20 mg (es)omeprazole, >20mg pantoprazole, >30mg lansoprazole, >20mg rabeprazole
[b] Some drugs contain considerable potassium amounts: Glucosamine in potassium salt (up to 300mg/tablet), oral nutritional supplements (up to 200mg/unit).... (Recommended Daily Dose: 3000mg/day for ≥60 year old patients)
[c] Some supplements such as oral nutritional supplements contain considerable Vitamin K amounts (up to 13µg/unit). (Recommended Daily Dose: 50-70µg/day for ≥60 year old patients)

Table 2: Drugs with high risk for anticholinergic (side-)effects (Adapted from Duran et al. (47))

High-potency anticholinergics		Low-potency anticholinergics		
Acepromazine	Hydroxyzine	Alimemazine	Fluoxetine	Prochlorperazine
Amitriptyline	Hyoscyamine	Amantadine	Fluvoxamine	Promazine
Atropine	Imipramine	Baclofen	Haloperidol	Quetiapine
Belladonna Alkaloids	Levomepromazine	Bromocriptine	Hydrocodone	Ranitidine
Brompheniramine	Meclozine	Carbamazepine	Ketorolac	Risperidone
Chlorphenamine	Nortriptyline	Cetirizine	Lithium	Temazepam
Chlorpromazine	Orphenadrine	Chlordiazepoxide	Loperamide	Theophylline
Clemastine	Oxybutynin	Cimetidine	Loratadine	Tramadol
Clomipramine	Procyclidine	Citalopram	Loxapine	Trazodone
Clozapine	Promethazine	Clonazepam	Meperidine (=Pethidine)	Triazolam
Cyproheptadine	Propantheline	Codeine	Methadone	
Darifenacin	Pyrilamine	Cyclobenzaprine	Methocarbamol	
Dexchlorpheniramine	Scopolamine	Diazepam	Mirtazapine	
Dicyclomine	Thioridazine	Digitoxin	Morphine	
Dimenhydrinate	Tizanidine	Disopyramide	Olanzapine	
Diphenhydramine	Tolterodine	Domperidone	Oxcarbazepine	
Doxepin	Trihexyphenidyl	Dosulepin	Oxycodone	
Flavoxate	Trimipramine	Entacapone	Paroxetine	
Fluphenazine	Tropatepine	Fentanyl	Phenelzine	
Homatropine		Fexofenadine	Pimozide	

***Remark**: Tiotropium and ipratropium not included because of low risk for systemic side-effects after inhalation.*

Table 3: Published lists, used as basis for the GheOP³S-tool.

	Part 1	Part 2	Part 3	Part 4	Part 5
Beers-list (2012 update) (10)	X	X		X	
Austrian list(12)	X				
Australian list(11)	X	X			
Laroche-criteria(13)	X			X	
Rancourt-criteria(14)	X			X	
PRISCUS-list(15)	X				
Lindblad-list(16)		X			
NORGEP-criteria(17)	X			X	
McLeod-criteria(18)	X	X		X	
IPET(19)	X	X			
START(20)			X		
STOPP(21)	X	X		X	
Winit-Watjana-criteria(22)	X	X		X	
Zhan-criteria(23)	X				
ACOVE-criteria(30)			X		X
HARM-Wrestling report(31)		X	X	X	X
KNMP-guidelines(32)		X			
Hines et al(33)				X	

***ACOVE:** Assessing Care of Vulnerable Elders; **HARM:** Hospital Admissions Related to Medication; **IPET:** improving prescribing in the elderly tool; **KNMP:** Koninklijke Nederlandse Maatschappij ter bevordering der Pharmacie **NORGEP:** Norwegian General Practice; **START:** screening tool to alert to right treatment; **STOPP:** screening tool of older people's prescriptions;*

Table 4: Flow of the items through the development process of the GheOP³S-tool.

	Part 1	Part 2	Part 3	Part 4	Part 5	Total
Number of different items retrieved in the literature	188	67	22	117	4	**398**
Number of items in literature-based list of potential items	53	33	7	24	4	**121**
Number of items added during the first Delphi round	13	1	3	5	6	**28**
Number of items in preliminary list of clinically relevant items	65	34	10	29	10	**148**
→ of which to be discussed in second Delphi round because of 'disagreement'	33	13	5	17	8	**76**
Number of items in final list of clinically relevant items	32	26	7	28	6	**99**
Number of items in the GheOP³S-tool	31	11	6	29	6	**83**

Table 5: Items deleted from each GheOP³S-part because of current inapplicability in the community pharmacy

Part 1: Drugs, inappropriate for older patients, independent of diagnosis

Sotalol for rate control

Part 2: Drugs, inappropriate for older patients, dependent on diagnosis

RAAS-inhibitors in renal impairment
Any potassium sparing diuretic in renal impairment
Chlortalidon and thiazides in renal impairment
Allopurinol in renal impairment
Amoxicillin with full dose clavulanic acid in renal impairment
Ciprofloxacin in renal impairment
Dabigatran in renal impairment
Digoxin in renal impairment
Diltiazem in congestive heart failure
Metformin in renal impairment
Nitrofurantoin in renal impairment
Norfloxacin in renal impairment
Sotalol in renal impairment
Verapamil in congestive heart failure

Part 3: PPOs for older patients

When a patients has elevated total cholesterol, a statin in secondary prevention should be started when the patient has a good life expectancy

Part 4: Drug-Drug interactions of specific relevance in older patients

None

Part 5: General care-related items for older patients to be addressed in the community pharmacy

None

REFERENCES

1. Pammolli F, Riccaboni M, Magazzini L. The sustainability of European health care systems: beyond income and aging. Eur J Health Econ. 2012;13(5):623-34.
2. Sikdar KC, Dowden J, Alaghehbandan R, MacDonald D, Wang PP, Gadag V. Adverse Drug Reactions in Elderly Hospitalized Patients: A 12-Year Population-Based Retrospective Cohort Study. Annals of Pharmacotherapy. 2012;46(7-8):960-71.
3. Gallagher P, Barry P, O'Mahony D. Inappropriate prescribing in the elderly. J Clin Pharm Ther. 2007;32(2):113-21.
4. Passarelli MCG, Jacob W, Figueras A. Adverse drug reactions in an elderly hospitalised population - Inappropriate prescription is a leading cause. Drugs & Aging. 2005;22(9):767-77.
5. Spinewine A, Schmader KE, Barber N, Hughes C, Lapane KL, Swine C, et al. Appropriate prescribing in elderly people: how well can it be measured and optimised? Lancet. 2007;370(9582):173-84.
6. Fu AZ, Jiang JZ, Reeves JH, Fincham JE, Liu GG, Perri M. Potentially inappropriate medication use and healthcare expenditures in the US community-dwelling elderly. Med Care. 2007;45(5):472-6.
7. Ryan C, O'Mahony D, Kennedy J, Weedle P, Byrne S. Potentially inappropriate prescribing in an Irish elderly population in primary care. British Journal of Clinical Pharmacology. 2009;68(6):936-47.
8. Opondo D, Eslami S, Visscher S, de Rooij SE, Verheij R, Korevaar JC, et al. Inappropriateness of Medication Prescriptions to Elderly Patients in the Primary Care Setting: A Systematic Review. PLoS One. 2012;7(8).
9. Kaur S, Mitchell G, Vitetta L, Roberts MS. Interventions that can reduce inappropriate prescribing in the elderly: a systematic review. Drugs Aging. 2009;26(12):1013-28.
10. Fick D, Semla T, Beizer J, Dombrowski R, Brandt N, DuBeau CE, et al. American Geriatrics Society Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2012;60(4):616-31.
11. Basger BJ, Chen TF, Moles RJ. Validation of prescribing appropriateness criteria for older Australians using the RAND/UCLA appropriateness method. BMJ open. 2012;2(5).
12. Mann E, Bohmdorfer B, Fruhwald T, Roller-Wirnsberger RE, Dovjak P, Duckelmann-Hofer C, et al. Potentially inappropriate medication in geriatric patients: the Austrian consensus panel list. Wien Klin Wochen. 2012;124(5-6):160-9.
13. Laroche ML, Charmes JP, Merle L. Potentially inappropriate medications in the elderly: a French consensus panel list. Eur J Clin Pharmacol. 2007;63(8):725-31.
14. Rancourt C, Moisan J, Baillargeon L, Verreault R, Laurin D, Gregoire JP. Potentially inappropriate prescriptions for older patients in long-term care. BMC geriatrics. 2004;4:9.
15. Holt S, Schmiedl S, Thurmann PA. Potentially Inappropriate Medications in the Elderly: The PRISCUS List. Dtsch Arztebl Int. 2010;107(31-32):543-U39.
16. Lindblad CI, Hanlon JT, Gross CR, Sloane RJ, Pieper CF, Hajjar ER, et al. Clinically important drug-disease interactions and their prevalence in older adults. Clin Ther. 2006;28(8):1133-43.
17. Rognstad S, Brekke M, Fetveit A, Spigset O, Wyller TB, Straand J. The Norwegian General Practice (NORGEP) criteria for assessing potentially inappropriate prescriptions to elderly patients. Scand J Prim Health Care. 2009;27(3):153-9.
18. McLeod PJ, Huang AR, Tamblyn RM, Gayton DC. Defining inappropriate practices in prescribing for elderly people: A national consensus panel. Can Med Assoc J. 1997;156(3):385-91.
19. Naugler CT, Brymer C, Stolee P, Arcese ZA. Development and validation of an improving prescribing in the elderly tool. The Canadian journal of clinical pharmacology = Journal canadien de pharmacologie clinique. 2000;7(2):103-7.
20. Barry PJ, Gallagher P, Ryan C, O'Mahony D. START (screening tool to alert doctors to the right treatment)an evidence-based screening tool to detect prescribing omissions in elderly patients. Age and Ageing. 2007;36(6):632-8.
21. Gallagher P, Ryan C, Byrne S, Kennedy J, O'Mahony D. STOPP (Screening Tool of Older Person's Prescriptions) and START (Screening Tool to Alert Doctors to Right Treatment). Consensus validation. Int J Clin Pharmacol Ther. 2008;46(2):72-83.
22. Winit-Watjana W, Sakulrat P, Kespichayawattana J. Criteria for high-risk medication use in Thai older patients. Arch Gerontol Geriatr. 2008;47(1):35-51.
23. Zhan CL, Sangl J, Bierman AS, Miller MR, Friedman B, Wickizer SW, et al. Potentially inappropriate medication use in the community-dwelling elderly - Findings from the 1996 Medical Expenditure Panel Survey. Jama-Journal of the American Medical Association. 2001;286(22):2823-9.
24. Lechevallier-Michel N, Gautier-Bertrand M, Alperovitch A, Berr C, Belmin J, Legrain S, et al. Frequency and risk factors of potentially inappropriate medication use in a community-dwelling elderly population: results from the 3C Study. Eur J Clin Pharmacol. 2005;60(11):813-9.
25. Ryan C, O'Mahony D, O'Donovan DO, O'Grady E, Weedle P, Kennedy J, et al. A comparison of the application of STOPP/START to patients' drug lists with and without clinical information. International journal of clinical pharmacy. 2013;35(2):230-5.
26. Galvin R, Moriarty F, Cousins G, Cahir C, Motterlini N, Bradley M, et al. Prevalence of potentially inappropriate prescribing and prescribing omissions in older Irish adults: findings from The Irish LongituDinal Study on Ageing study (TILDA). European journal of clinical pharmacology. 2014;70(5):599-606.
27. Maio V, Yuen EJ, Novielli K, Smith KD, Louis DZ. Potentially inappropriate medication prescribing for elderly outpatients in Emilia Romagna, Italy: a population-based cohort study. Drugs Aging. 2006;23(11):915-24.
28. Fick DM, Mion LC, Beers MH, Waller JL. Health Outcomes Associated With Potentially Inappropriate Medication Use in Older Adults. Research in nursing & health. 2008;31(1):42-51.
29. Fitch K, Bernstein SJ, Aguilar MS, Burnand B, LaCalle JR, Lazaro P, et al. The RAND/UCLA Appropriateness Method User's Manual [cited 2014 April 14th]. Available from: http://www.rand.org/pubs/monograph_reports/MR1269.html.
30. ACOVE quality indicators. Ann Intern Med. 2001;135(8):653-67.
31. Ministry of Health WS. HARM-Wrestling report: a proposition from the expert group Medication Safety concerning specific intervention improving extramural medication safety on a short-term. 2009.
32. KNMP. Labwaarden en Nierfunctie, uitwisseling van gegevens 2011. Available from: http://www.knmp.nl/downloads/samenwerken-kennis-delen/innovatieve-apotheken/LabwaardenenNierfunctieuitwisselingvangegevens.pdf.

33. Hines LE, Murphy JE. Potentially Harmful Drug-Drug Interactions in the Elderly: A Review. Am J Geriatr Pharmacother. 2011;9(6):364-77.
34. Pharmaceutical Care Unit. Ghent Older People's Prescriptions community Pharmacy Screening tool: Rationales, management plans and additional information. 2014. Available from: http://www.ugent.be/fw/nl/onderzoek/bioanalyse/farmzorg/tools.htm/gheops.htm.
35. Price SD, Holman CD, Sanfilippo FM, Emery JD. Association between potentially inappropriate medications from the Beers criteria and the risk of unplanned hospitalization in elderly patients. The Annals of pharmacotherapy. 2014;48(1):6-16.
36. Lund BC, Carnahan RM, Egge JA, Chrischilles EA, Kaboli PJ. Inappropriate prescribing predicts adverse drug events in older adults. The Annals of pharmacotherapy. 2010;44(6):957-63.
37. World Health Organization. The role of the pharmacist in the health care system 1994 [cited 2014 June 3]. Available from: http://apps.who.int/medicinedocs/en/d/Jh2995e/.
38. European Directorate for the Quality of Medicines & HealthCare. Pharmaceutical Care - Policies and Practices for a Safer, More Responsible and Cost-effective Health System: Dr S. Keitel; 2012 [cited 2014 June 3]. Available from: http://www.edqm.eu/en/pharmaceutical-care-1517.html.
39. Kwint HF, Faber A, Gussekloo J, Bouvy ML. Completeness of medication reviews provided by community pharmacists. J Clin Pharm Ther. 2014;39(3):248-52.
40. Olesen C, Harbig P, Barat I, Damsgaard EM. Absence of 'over-the-counter' medicinal products in on-line prescription records: a risk factor of overlooking interactions in the elderly. Pharmacoepidemiol Drug Saf. 2013;22(2):145-50.
41. Cahir C, Bennett K, Teljeur C, Fahey T. Potentially inappropriate prescribing and adverse health outcomes in community dwelling older patients. Br J Clin Pharmacol. 2014;77(1):201-10.
42. Nyborg G, Straand J, Brekke M. Inappropriate prescribing for the elderly--a modern epidemic? European journal of clinical pharmacology. 2012;68(7):1085-94.
43. Barnett K, McCowan C, Evans JM, Gillespie ND, Davey PG, Fahey T. Prevalence and outcomes of use of potentially inappropriate medicines in older people: cohort study stratified by residence in nursing home or in the community. BMJ quality & safety. 2011;20(3):275-81.
44. Gallagher PF, O'Connor MN, O'Mahony D. Prevention of Potentially Inappropriate Prescribing for Elderly Patients: A Randomized Controlled Trial Using STOPP/START Criteria. Clin Pharmacol Ther. 2011;89(6):845-54.
45. McMullin ST, Hennenfent JA, Ritchie DJ, Huey WY, Lonergan TP, Schaiff RA, et al. A prospective, randomized trial to assess the cost impact of pharmacist-initiated interventions. Arch Intern Med. 1999;159(19):2306-9.
46. Pitkala KH, Strandberg TE, Tilvis RS. Inappropriate drug prescribing in home-dwelling, elderly patients: a population-based survey. Arch Intern Med. 2002;162(15):1707-12.
47. Duran CE, Azermai M, Vander Stichele RH. Systematic review of anticholinergic risk scales in older adults. Eur J Clin Pharmacol. 2013;69(7):1485-96.
48. World Health Organization Collaborating Centre for Metabolic Bone Diseases. Fracture Risk Assessment Tool United Kingdom: University of Sheffield. Available from: https://www.shef.ac.uk/FRAX/tool.jsp.